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Recent studies show that women also suffer from aggression disorders and might exhibit severer symptomatology and comorbidity compared to men. Thus, novel animal models are needed to understand the neural underpinnings of aggression in both sexes. Here I will show how a fine-tuned balance between the release of the hypothalamic neuropeptides oxytocin and vasopressin, within the lateral septum, orchestrates aggression in female rats.

When the love hormone drives you mad: the interplay between oxytocin and vasopressin regulates female aggression

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In contrast to males, aggression in females has been rarely studied. Here, we aimed to establish a rat model of female aggression to study the neurobiological mechanisms underlying aggression in females, focusing specifically on the oxytocin (OXT) and arginine-vasopressin (AVP) systems. To do so, we used a combination of social isolation and aggression-training, i.e. repeated exposure to a same-sex intruder in the female intruder test, to enhance the mild levels of aggression displayed by virgin female Wistar rats. After having established the animal model, we employed neuropharmacological, optogenetic, chemogenetic as well as microdialyses approaches to reveal the role of the OXT and AVP systems on female aggression, focusing particularly on the lateral septum (LS). Social isolation and aggression-training were found to reliably exacerbate the aggression displayed by group-housed female rats. Additionally, elevated OXT release within the ventral LS (vLS), combined with reduced AVP release within the dorsal LS (dLS), was found to underly the high levels of aggression displayed by isolated and trained females. Precisely, OXT binding to OXT receptors (OXTRs) within the vLS promoted whereas AVP binding to V1a receptors within the dLS reduced aggression. Hence, increased activity of vLS neurons, as well as decreased activity dLS neurons, were required for female aggression. Finally, we have shown that in vitro activation of OXT receptors in the vLS differentially affected GABAergic tonic inhibition within the LS sub-networks, i.e. activation of OXTRs decreased the inhibitory spontaneous activity ventrally, whereas it increased it dorsally.

Altogether, our data reveal that female aggression is regulated by an intricate balance between OXT and AVP release in distinct regions of the LS. Furthermore, we suggest a model where the contrasting effects of those neuropeptides on aggression are determined by alterations in GABAergic neurotransmission within LS subnetworks.